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Case report

A breath from Houdini – A case of giant bullous emphysema

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A B S T R A C T

We describe a case of a young man presenting with exertional dyspnea. His chest radiograph showed hyperlucency in his left lung, and he was subsequently diagnosed to have giant bullous emphysema. An approach to lesions of decreased attenuation on computed tomography of the chest, with a focus on cystic lung diseases is discussed. This is followed by a literature review of the clinical presentation, natural history, radiology and management of giant bullous emphysema. Although this is an uncommon condition, a clinician has to be cognizant of the fact that it may mimic other common respiratory diseases. This review highlights the importance of these caveats as misguided treatment options may lead to devastating consequences.

Case report

A 37-year-old Indonesian man presented to the respiratory clinic for exertional dyspnea that had bothered him for a year.

A diagnosis of bronchiectasis was made in 2008 by his doctors back home, based on a history of chronic productive cough and a compatible chest radiograph. There was no history of any severe respiratory infection in childhood, and he had generally been in good health all his life. He was a never smoker, and denied any exposure to environmental tobacco smoke or biomass fuel. He worked as an engineer, which was the only job he had ever held. He did have any exposure to biological or industrial dusts, gases and fumes. He led a sedentary lifestyle, and had never taken any recreational drugs. There was no family history of respiratory illnesses.

He remained well until 2010 when he began to feel breathless on exertion. This was not associated with chest pain, orthopnea, paroxysmal nocturnal dyspnea or lower limb swelling. He denied any significant cough, hemoptysis or wheezing. He did not have constitutional symptoms such as fever, night sweats, anorexia or weight loss. He also did not have any skin or joint complaints. A repeat chest radiograph at this juncture (Fig. 1) revealed increased lucency in the upper half of the left hemithorax. This was followed by a chest computed tomography (CT) scan that revealed bronchiectatic changes in the left lower lobe with a few small cysts and several bullae occupying almost the entire left hemithorax (Fig. 2). Extensive blood investigations including immunoglobulin levels, connective tissue disease screen and alpha-1 antitrypsin level were unremarkable. Spirometry showed a forced expiratory volume in 1 s (FEV1) to forced vital capacity (FVC) ratio of 0.83, FVC of 2.56 L (59% of predicted), and FEV1 of 2.13 L (59% or predicted). Bronchodilator reversibility testing was not performed. Total lung capacity (TLC) measured via nitrogen washout method and body plethysmography showed an unsurprising discrepancy in results; TLC measured 3.43 L (56% of predicted) and 5.33 L (88% of predicted) respectively. However, the residual volume of 2.65 L (156% of predicted) suggested the presence of significant air trapping, making dynamic hyperinflation the most probable physiological explanation for the patient's breathlessness. Carbon monoxide diffusion capacity, adjusted for hemoglobin was unremarkable at 77% of predicted.

On examination, his vital signs were stable. He had a heart rate of 70 beats per minute, and a blood pressure of 120/80. The respiratory rate was 18 breaths per minute, with an oxygen saturation of 98% on ambient air. He was of medium build and was not distressed at rest. No clubbing was noted in his fingers. Respiratory examination revealed a centrally located trachea, and reduced breath sounds over the left upper chest with a dull percussion note.

Bronchoscopy was grossly normal. There were no endobronchial lesions. Malacia was seen in the apico-posterior segment of the left upper division, and the left lower lobe bronchopulmonary segments appeared mildly dilated (Fig. 3). Bronchoalveolar lavage (BAL) was performed in the left lower lobe; there was no alveolar

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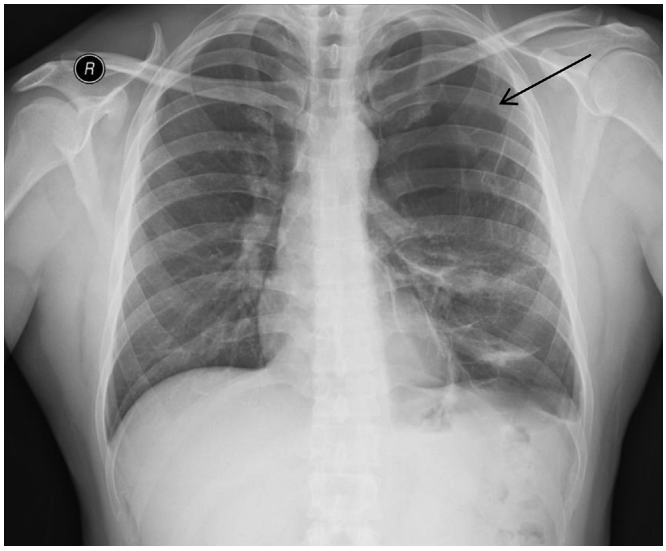

Fig. 1. Chest radiograph – increased lucency (arrow) in left upper zone, with increased interstitial markings in left lower zone.

hemorrhage, and cultures for pyogenic and mycobacterial organisms were negative. Cytology smears from BAL showed foamy alveolar macrophages and scattered polymorphs. Random endobronchial biopsies were taken from bronchial mucosa in the left upper lobe, and histology yielded fragments of bronchial mucosa with acute inflammation and mucosal erosions. There was no evidence of granulomatous inflammation or malignancy.

In view of his chest CT findings, he was diagnosed to have giant bullous emphysema (GBE).

Discussion

Our case of GBE is made interesting by its radiological findings of co-existing parenchymal lesions with seemingly similar morphology, as well as the fact that the patient was a never smoker. We will elaborate on the radiological approach we undertook to arrive at the diagnosis, following which a succinct literature review of GBE will be presented.

This patient's CT images demonstrated the co-existence of multiple parenchymal abnormalities comprising bronchiectasis, cysts and bullae. In this instance, the importance of proper nomenclature in describing such findings cannot be overemphasized. On chest CT, lesions of decreased attenuation are described as emphysema, honeycombing or cysts. Emphysema lacks visible walls, and often has a centrilobular and upper lobe predisposition. In contrast, honeycombing is characterized by thick walled cysts 3–10 mm thick which are aligned in one or more rows. Compared to honeycombing, cysts have thinner walls that are usually no more than 2 mm in thickness. Bullae are large cysts, and their walls may be formed by septa, pleura or compressed lung tissues. The differential diagnoses of cystic lung diseases are myriad, and include lymphangioleiomyomatosis (LAM), langerhans cell histiocytosis (LCH), Birt-Hogg-Dube Syndrome and lymphoid interstitial pneumonia (LIP).

The various cystic lung diseases can be differentiated from one another by the character and distribution of pulmonary cysts. The cysts in LAM are typically uniform and affect both lungs diffusely while those in LCH are irregularly shaped, preferentially affect upper lobes, and are often associated with nodules. The presence of chylous pleural effusions and pneumothoraces will also favor the diagnosis of LAM [1,2]. Birt-Hogg-Dube (BHD) syndrome causes pulmonary cysts which are similar in appearance to those in LAM.

Fig. 2. CT chest – large bullae in both left upper and lower lobes, with co-existing bronchiectasis (thin arrow) and cysts (bold arrow).

However, these cysts tend to affect lung bases, and may be associated with non-pulmonary manifestations such as renal cysts, malignant renal tumors, and benign tumors of the hair follicles [3]. In LIP, cysts are typically found in a bronchovascular and subpleural distribution, and are often associated with centrilobular nodules, ground glass changes and interlobular septal thickening [4].

What is striking about the radiographic findings in this patient is the marked asymmetrical pattern of involvement, with large bullae preferentially affecting and almost obliterating the entire left hemithorax. Some cysts and areas of bronchiectasis are seen in the

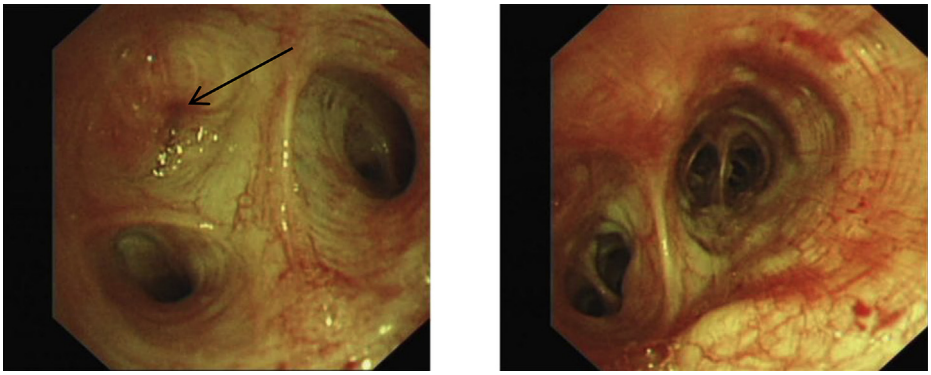

Fig. 3. Malacia of apico-posterior segment of left upper division (thin arrow) (left); left lower lobe bronchopulmonary segments mildly dilated (right).

ipsilateral lung but there are no suggestive features of the cystic lung diseases discussed earlier. Therefore, the most likely diagnosis is GBE.

Idiopathic GBE is a disorder characterized by bullae occupying more than a third of the hemithorax, and mostly affects men who are smokers [5]. It has been sporadically described in radiological and surgical journals since the first case report by Burke in 1937 [6]. This condition is also known by other names such as type 1 bullous disease, primary bullous disease of the lung and vanishing lung syndrome. Vanishing lung syndrome can be traced back to more than 70 years ago, when Burke published "Vanishing lungs: a case of bullous emphysema" in the journal Radiology.

The prevalence of this condition remains unknown, as only small case series have been reported worldwide. Its cause is obscure, but it has been observed to have a male predisposition, and occurs mostly in smokers [7,8]. It has been postulated that smoking upsets the balance in alveolar proteases and antiproteases, causing a chain reaction at the cellular level that eventually leads to destruction of alveolar walls. More recently, oxidative stress resulting from an imbalance between oxidant and antioxidant proteins has also been implicated [9]. It is perhaps timely to reiterate at this juncture the absence of cigarette smoking in our case. There has been no conclusive evidence with regards to the development of GBE in non-smokers. However, it may not be unreasonable to assume that different triggers (congenital or acquired) other than cigarette smoke incite the same cascade of subcellular inflammatory mediators, and thus upsets the balance of proteases/antiproteases and oxidants/antioxidants in the lung. The corollary of this chain reaction is the same – destruction of alveolar walls resulting in permanent and abnormal enlargement of distal airspaces i.e. emphysema. Supporting this hypothesis are reports of hereditary alpha-1 antiproteases in non-smokers who present in a fashion not dissimilar to GBE [10]. Interestingly, infrequent associations with medical conditions (e.g. sarcoidosis and systemic lupus erythematous), recreational drug abuse (e.g. intravenous methylphenidate, cocaine and marijuana), and lung cancer have also been described [11–17].

Although sporadic resolution of bullae has been infrequently reported, with one notable case of regression after bronchodilator treatment, the natural history of GBE appears to be a largely progressive one [18,19]. The rate of progression is, however, highly variable. Enlarging bullae cause symptoms by interfering with respiratory mechanics and gas exchange. As they grow larger, they compress on normal lung parenchyma, reduce lung compliance, and increase work of breathing. As dead space fraction increases with bullae formation, gas exchange is also impaired [8].

Complications of this condition include the development of pneumothoraces, infection of existing bullae, and progression to respiratory failure [20]. It can prove to be a diagnostic challenge when patients with undiagnosed GBE present with acute breathlessness to the emergency department. A chest radiograph may not be reliable enough to differentiate a pneumothorax from a giant bulla, especially without a previous one for comparison [21]. In such an instance, a chest CT scan should then be considered, as insertion of a chest drain into a bulla can lead to catastrophic consequences such as an iatrogenic pneumothorax, hemothorax and death.

A chest CT typically reveals numerous cysts that can vary greatly in size, from 1 cm to bullae large enough to occupy the entire hemithorax. It has been noted from case series that the condition has a propensity to affect the upper lobes, and often presents with bilateral involvement, albeit in an asymmetric fashion [8]. Paraseptal emphysema is the predominant CT finding; this then leads to the formation of subpleural cysts and bullae [8]. Not surprisingly, centrilobular emphysema often co-exists, given the strong association with cigarette smoking [22]. Occasionally, CT may detect bronchiectasis or pulmonary hypertension [22]. The detection of nodules, thickened bulla wall, increasing bulla size, and fluid filled bulla should raise the suspicion of an underlying lung malignancy [17].

In addition to general measures such as smoking cessation and vaccinations, the treatment of choice in GBE is bullectomy. In a prospective case series of 41 patients with GBE undergoing elective bullectomy, the procedure has been shown to improve symptoms and lung function up to 5 years, without new bullae formation or enlargement of pre-existing bullae at the surgical site [23]. There was no mortality difference between open thoracotomy and video-assisted thoracoscopic surgery. Higher mortality rates and negation of the effects of bullectomy at 5 years were found only in patients with diffuse emphysema. If surgery is not performed, close surveillance is recommended given the association with lung cancer [24]. However, there remains no consensus on the ideal timing for surgery, or follow up of these patients.

It is generally accepted that bullectomy be best offered electively to markedly symptomatic patients without underlying diffuse emphysema. The role of spirometry in guiding therapy remains unclear. Firstly, it appears that patients with more severely impaired preoperative FEV1 are less likely to benefit from bullectomy, especially if the FEV1 is less than 35% [25,26]. However, a successful case of marked improvement in FEV1 has been reported recently after bullectomy [27]. Secondly, GBE is not necessarily associated with an obstructive pathology, as clearly demonstrated by this case. This same fact also explains the limited utility of spirometry in the follow up of this condition. As comprehensive lung function tests are often performed in the diagnostic work up, it must be reiterated that total lung capacity should be measured via

body plethysmography due to volume underestimation using gas dilution methods.

As for our patient, he is being monitored closely for worsening symptoms, with an intention for bullectomy if his condition worsens. His symptoms have been managed adequately with bronchodilators. A repeat spirometry performed on follow up was largely unchanged from before. It is fortunate that his symptoms and effort tolerance have remained largely stable on subsequent clinic visits.

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